

IN THE CLAIMS

This listing of claims will replace all prior versions and listings of the claims in the present application.

Please cancel, without prejudice, claim 124.

1-12. **(Cancelled)**

13. **(Currently amended)** A method for inducing or enhancing the glucose-responsiveness of a pancreatic cell, which pancreatic cell has impaired cell function and which cell function is glucose-responsiveness, comprising administering to said the pancreatic cell an amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to induce or enhance the glucose-responsiveness of said the pancreatic cell, and wherein said PYY agonist or biologically active fragment thereof binds a PYY receptor and promotes glucose-responsiveness of said the pancreatic cell.

14. **(Cancelled)**

15. **(Currently amended)** The method of claim 13, whereby administration of the PYY agonist causes the cell to produce insulin when ~~treated~~contacted with glucose.

16. **(Previously presented)** The method of claim 13, wherein the cell is a fetal islet cell.

17. **(Original)** The method of claim 13, wherein the cell is a fetal pancreatic cell.

18. **(Previously presented)** The method of claim 13, wherein the cell is a postpartum islet cell.

19. **(Previously presented)** The method of claim 13, wherein the cell is a postpartum cell.
20. **(Previously presented)** The method of claim 13, wherein the cell is a pancreatic β cell.
21. **(Currently amended)** A method for inducing or enhancing glucose metabolism in an animal having a disease associated with abnormal glucose metabolism, comprising administering to ~~said~~the animal ~~an amount of~~ a composition including an amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, ~~and~~ wherein the amount of said PYY agonist or biologically active fragment thereof is therapeutically effective to induce or enhance glucose metabolism in ~~said~~the animal, and wherein said PYY agonist or biologically active fragment thereof binds a PYY receptor and alleviates at least one adverse effect or symptom of said disease associated with abnormal glucose metabolism.
22. **(Cancelled)**
23. **(Currently amended)** A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism ~~an amount of~~ a composition comprising an amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, ~~and~~ wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to treat the disease, and wherein said PYY agonist or biologically active fragment binds a PYY receptor and alleviates at least one adverse effect or symptom of said disease associated with altered glucose metabolism.

24-27. (Cancelled)

28. (Previously presented) The method of claim 23, wherein said disease is a condition selected from insulin resistance, glucose intolerance or glucose non-responsiveness.

29. (Previously presented) The method of claim 23, wherein said disease is Type II diabetes mellitus (NIDD).

30. (Currently amended) The method of any one of claims 13 and 15-20, wherein said PYY agonist is administered together with at least one of a dipeptidylpeptidase inhibitor, insulin, or GLP-1.

31. (Currently amended) The method of any one of claims 13 and 15-20, wherein said PYY agonist is conjointly administered either simultaneously, sequentially, or separately with at least one of a dipeptidylpeptidase inhibitor, insulin, or GLP-1.

32. (Previously presented) The method of claim 30, wherein said dipeptidylpeptidase inhibitor is DPIV.

33. (Currently amended) A method for maintaining or restoring a function of a pancreatic β cell, wherein the function is glucose responsivity or glucose sensing, comprising administering to a pancreatic cell, which pancreatic cell has impaired glucose responsivity or glucose sensing, a composition comprising an amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain or restore the function of said pancreatic β cell, and wherein said PYY agonist or biologically active fragment binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

34-38. (Cancelled)

39. (Previously presented) The method of any one of claims 13 and 15-20, wherein said PYY agonist enhances or recovers glucose responsiveness.

40-44. (Cancelled)

45. (Currently amended) A method for maintaining or restoring normal pancreatic function to a pancreatic cell having impaired pancreatic cell function, wherein the function is glucose responsivity or glucose sensing, comprising administering to a cultured pancreatic cell having altered pancreatic cell function an amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain or restore normal pancreatic cell function to a pancreatic cell having altered pancreatic cell function, and wherein said PYY agonist or biologically active fragment binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

46. (Previously presented) The method of claim 45, wherein the pancreatic cell is a failing β cell.

47-49. (Cancelled)

50. (Previously presented) The method of claim 21, wherein said animal is selected from the group consisting of a human and a rat.

51-52. (Cancelled)

53. (Previously presented) The method of claim 17, wherein the cell is a pancreatic β cell.

54. **(Previously presented)** The method of claim 19, wherein the cell is a pancreatic β cell.

55-56. **(Cancelled)**

57. **(Currently amended)** The method of claim 21, wherein said composition further comprises at least one of a dipeptidylpeptidase inhibitor, insulin or GLP-1.

58. **(Currently amended)** The method of claim 21, wherein said composition is conjointly administered either simultaneously, sequentially or separately with at least one of a dipeptidylpeptidase inhibitor, insulin or GLP-1.

59. **(Currently amended)** The method of claim 23, wherein said composition further comprises at least one of a dipeptidylpeptidase inhibitor, insulin or GLP-1.

60. **(Currently amended)** The method of claim 23, wherein said composition is conjointly administered either simultaneously, sequentially or separately with at least one of a dipeptidylpeptidase inhibitor, insulin or GLP-1.

61-75. **(Cancelled)**

76. **(Previously presented)** The method of claim 23, wherein said PYY agonist enhances or recovers glucose responsiveness.

77. **(Previously presented)** The method of claim 21, wherein said PYY agonist enhances or recovers glucose responsiveness.

78. **(Previously presented)** The method of claim 33, wherein said PYY agonist enhances or recovers glucose responsiveness.

79-84. (Cancelled)

85. (Previously presented) The method of claim 23, wherein said animal is selected from the group consisting of a human and a rat.

86. (Cancelled)

87. (Currently amended) A method for inducing or enhancing the glucose-responsiveness of a pancreatic cell, which pancreatic cell has impaired glucose-responsiveness, comprising administering to ~~said the~~ pancreatic cell an amount of a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to induce or enhance the glucose-responsiveness of ~~said the~~ pancreatic cell, wherein the PYY or biologically active fragment thereof binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

88. (Currently amended) A method for inducing or enhancing glucose metabolism in an animal having a disease associated with abnormal glucose metabolism, comprising administering to ~~said the~~ animal ~~an effective amount of~~ a composition including an amount of a PYY or a biologically active fragment thereof, wherein the amount of PYY or a biologically active fragment thereof is effective to induce or enhance glucose responsiveness in ~~said the~~ animal, thereby inducing or enhancing glucose metabolism in ~~said the~~ animal, and wherein the PYY or biologically active fragment thereof binds a PYY receptor and alleviates at least one adverse effect or symptom of said disease associated with abnormal glucose metabolism.

89. (Currently amended) A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism ~~an amount of~~ a composition comprising an amount of a PYY or a biologically active fragment thereof, wherein the amount of PYY or a biologically active fragment thereof is sufficient to treat the disease in ~~said the~~ animal, and wherein the PYY or

biologically active fragment thereof binds a PYY receptor and alleviates at least one adverse effect or symptom of said disease associated with altered glucose metabolism.

90. **(Currently amended)** A method for maintaining or restoring a function of a pancreatic β cell, wherein the function is glucose responsivity or glucose sensing, comprising administering to a pancreatic cell, which pancreatic cell has impaired glucose responsivity or glucose sensing, a composition comprising an amount of a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to maintain or restore the function of said pancreatic β cell, wherein the PYY or biologically active fragment thereof binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

91. **(Currently amended)** A method for maintaining or restoring normal pancreatic cell function, wherein the function is glucose responsivity or glucose sensing, comprising administering to a cultured pancreatic cell, which pancreatic cell has impaired glucose responsivity or glucose sensing, an amount of a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to maintain or restore normal pancreatic cell function, wherein the PYY or biologically active fragment thereof binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

92. **(Currently amended)** A method for maintaining glucose-responsiveness of a pancreatic cell, comprising contacting the pancreatic cell, which pancreatic cell has impaired glucose responsivity or glucose sensing, with a composition comprising an amount of a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to maintain the glucose-responsiveness of the pancreatic cell, wherein the PYY or biologically active fragment thereof binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

93. **(Currently amended)** A method for maintaining glucose-responsiveness of a pancreatic cell, which pancreatic cell has impaired glucose-responsiveness, comprising contacting said the pancreatic cell with ~~an effective amount of~~ a composition comprising an amount of a PYY

agonist or a biologically active fragment thereof, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain the glucose responsiveness of said the pancreatic cell, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, and wherein said PYY agonist, or biologically active fragment binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

94. **(Currently amended)** A method for inducing, enhancing, or maintaining glucose-responsiveness of a pancreatic cell, which pancreatic cell has impaired glucose-responsiveness, comprising contacting said the pancreatic cell with ~~an effective amount of~~ a composition comprising an amount of a PYY agonist or a biologically active fragment thereof, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to induce, enhance, or maintain the glucose-responsiveness of said the pancreatic cell, wherein said PYY agonist comprises a polypeptide at least 70% identical with SEQ ID NO: 3, and wherein said PYY agonist, or biologically active fragment binds a PYY receptor and promotes glucose-responsiveness of said pancreatic cell.

95. **(Cancelled)**

96. **(Previously presented)** The method of claim 94, wherein the PYY agonist comprises a polypeptide at least 80% identical to SEQ ID NO: 3.

97. **(Previously presented)** The method of claim 94, wherein the PYY agonist comprises a polypeptide at least 85% identical to SEQ ID NO: 3.

98. **(Previously presented)** The method of claim 94, wherein the PYY agonist comprises a polypeptide at least 90% identical to SEQ ID NO: 3.

99. **(Cancelled)**

100. **(Currently amended)** The method of any one of claims 92-94, wherein the pancreatic cell is a α , β , δ , or ϕ -cell.

101. **(Currently amended)** The method of any one of claims 92-94, wherein the pancreatic cell is an insulin-producing cell.

102. **(Currently amended)** A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism ~~an amount of~~ a composition comprising an ~~effective~~ amount of a PYY agonist or a biologically active fragment thereof effective to treat said disease associated with altered glucose metabolism, wherein said PYY agonist comprises a polypeptide at least 70% identical to SEQ ID NO: 3, and wherein said PYY agonist, or biologically active fragment binds a PYY receptor and alleviates at least one adverse effect or symptom of said disease associated with altered glucose metabolism.

103. **(Previously presented)** The method of claim 102, wherein the PYY agonist comprises a polypeptide at least 80% identical to SEQ ID NO: 3.

104. **(Previously presented)** The method of claim 102, wherein the PYY agonist comprises a polypeptide at least 85% identical to SEQ ID NO: 3.

105. **(Previously presented)** The method of claim 102, wherein the PYY agonist comprises a polypeptide at least 90% identical to SEQ ID NO: 3.

106. **(Currently amended)** The method of any one of claims 102, ~~103 and~~ to 105, wherein said disease is a condition selected from insulin resistance, glucose intolerance or glucose non-responsiveness.

107. **(Currently amended)** The method of any one of claims 102,~~103~~ and to 105, wherein said disease is hyperglycemia.
108. **(Previously presented)** The method of any one of claims 102 to 105, wherein said disease is obesity.
109. **(Currently amended)** The method of any one of claims 102,~~103~~ and to 105, wherein said at least one adverse effect or symptom of said disease associated with altered glucose metabolism ~~disease is comprises~~ hyperlipidemia or hyperlipoproteinemia.
110. **(Previously presented)** The method of claim 23, wherein said disease is hyperglycemia.
111. **(Previously presented)** The method of claim 23, wherein said disease is obesity.
112. **(Currently amended)** The method of claim 23, wherein said at least one adverse effect or symptom of said disease associated with altered glucose metabolism ~~disease is comprises~~ hyperlipidemia or hyperlipoproteinemia.
- 113-115. **(Cancelled)**
116. **(Previously presented)** The method of claim 89, wherein said disease is a condition selected from insulin resistance, glucose intolerance or glucose non-responsiveness.
117. **(Previously presented)** The method of claim 89, wherein said disease is hyperglycemia.
118. **(Previously presented)** The method of claim 89, wherein said disease is obesity.
119. **(Currently amended)** The method of claim 89, wherein said at least one adverse effect or symptom of said disease associated with altered glucose metabolism ~~disease is comprises~~ hyperlipidemia or hyperlipoproteinemia.

120. **(Currently amended)** The method of any one of claims 89, and 102, ~~103 and to 105~~, wherein the composition further comprises GLP-1.
121. **(Currently amended)** The method of any one of claims 23, 89, and 102, ~~103 and to 105~~, wherein the treatment comprises nasal administration of the composition.
122. **(Currently amended)** The method of any one of claims 23, 89, and 102, ~~103 and to 105~~, wherein the PYY agonist or fragment is PYY(3-36) of SEQ ID NO: 3.
123. **(Currently amended)** The method of claim 118, wherein the biologically active fragment is PYY(3-36), the composition further comprises GLP-1, and the treatment comprises nasal administration of the composition.
124. **(Cancelled)**
125. **(Currently amended)** The method according to any one of claims 21, 23, ~~33, 45, 87, 88, 89, 90, 91, 92, 93, 94~~, or 102 wherein said PYY agonist or biologically active fragment also promotes glucose-responsiveness of pancreatic cells.
126. **(Previously presented)** The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also inhibits intestinal motility.
127. **(Previously presented)** The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also inhibits mesenteric blood flow.

128. **(Previously presented)** The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also mediates gastric, pancreatic, or intestinal exocrine secretion.

129. **(Previously presented)** The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also stimulates net absorption of nutrients.

130. **(Currently amended)** A method for maintaining or restoring a function of a pancreatic islet, wherein the function is glucose responsivity or glucose sensing, comprising administering to a pancreatic islet, which pancreatic islet has impaired glucose responsivity or glucose sensing, a composition comprising an amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain or restore the function of said pancreatic islet, and wherein said PYY agonist or biologically active fragment binds a PYY receptor and promotes glucose-responsiveness of said pancreatic islet.